

Chen and Chiou Respond to "Arsenic and Cancer of the Urinary Tract" by Cantor

Chien-Jen Chen¹ and Hung-Yi Chiou²

In his commentary (1) on our paper (2), Cantor has provided an excellent summary of the current state of knowledge on ingested arsenic and cancer risk. He has also highlighted a number of important issues regarding the epidemiologic study of risk of arsenic-induced cancers due to arsenic in drinking water. We shall briefly address several of his comments.

As Cantor points out, there is an urgent need to reassess the maximum contamination level of arsenic in drinking water. Global environmental change, rapid population growth, and manmade pollution have led to a shortage of available surface water for drinking and cooking in many countries. In more and more areas, underground water is being used as the main source of water for daily consumption. Since arsenic is a ubiquitous element in the earth's crust and is abundant in well water, arseniasis is becoming an emerging epidemic in several Asian countries (3).

Epidemiologic studies on skin cancer carried out in southwestern Taiwan have long been used for risk assessment of arsenic in drinking water (4). Because the water of shallow wells in this arseniasis-endemic area had a high salt content, rather than microbial contamination as observed in Bangladesh and West Bengal, India, residents in the area had used high-arsenic artesian well water from the early 20th century to the 1970s. There was a striking difference in the arsenic levels of water obtained from shallow wells and artesian wells. Since vital statistics were collected at the village level and there were several wells in each village that were shared by villagers, the median arsenic level of water in the wells of a given village was used as the exposure information. In our earlier studies on arsenic and internal cancer (5, 6), we grouped arsenic levels in well water into three broad groups: <300, 300–599, and ≥600 µg/liter. In a reanalysis of cancer mortality using more refined exposure levels, we found that the current maximum contamination level of 50 µg/liter is associated with a substantial excess risk of cancer and is not sufficiently protective of public health (7, 8).

However, the data from southwestern Taiwan had two limitations, as Cantor noted: 1) use of the median level of arsenic during the 1960s as the exposure dose and 2) use of mortality rather than incidence to estimate cancer risk.

Our current study in northeastern Taiwan (2) provided better measurement of arsenic levels in individual households. Furthermore, we used incidence rather than mortality to assess the risk of transitional cell carcinoma. As Cantor mentioned, our conclusions were indeed based on the assumption that current or recent measures of arsenic in water from these wells could represent long term historical levels. We conducted retests of arsenic levels in the water of randomly sampled wells. The correlation for the repeated measurements was quite high. Although 2,199 (26 percent) of the study subjects had changed wells at some time prior to study enrollment, they had used their current wells for approximately 60 percent (standard deviation 21) of their life span. In other words, most of them had used their current wells for at least 10 years.

There is indeed individual susceptibility to arsenic-induced health hazards. Undernourishment, liver dysfunction, poor arsenic methylation capability, and low serum levels of antioxidant vitamins have been found to increase the risk of arsenic-related vascular diseases and skin cancer (9–12). Genetic polymorphisms of glutathione *S*-transferases M1, T1, and P1 and several DNA repair enzymes were recently found to modify the risks of skin cancer and transitional cell carcinoma induced by arsenic (13–15). Both acquired and genetic susceptibility must be taken into consideration in assessment of the risk of arsenic.

Inorganic arsenic is readily absorbed through ingestion and is widely distributed in the human body. It does not require metabolic activation to exert its effects. The health hazards of arsenic do not show any unique organotropism. In addition to various malignant neoplasms and circulatory diseases (16, 17), arsenic has been documented to induce diabetes mellitus and lens opacity (18, 19). Diseases other than cancer must be considered in setting the maximum contamination level of inorganic arsenic in drinking water.

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¹Graduate Institute of Epidemiology, College of Public Health, National Taiwan University, Taipei, Taiwan.

²Department of Public Health, College of Medicine, Taipei Medical University, Taipei, Taiwan.

Reprint requests to Prof. Chien-Jen Chen, 1 Jen-Ai Road, Section 1, Taipei 10018, Taiwan (e-mail: cjchen@ha.mc.ntu.edu.tw).

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